United States
Environmental Protection
Agency

Office of Prevention, Pesticides
and Toxic Substances
(7501C)

Pesticide Fact Sheet

Name of Chemical: Boscalid
Reason for Issuance: New Chemical
Date Issued: July 2003

Description of Chemical

Chemical Name:
3-pyridinecarboxamide, 2-chloro-N-(4'chloro[1,1'biphenyl]-2-yl)

Common Name: Boscalid (BAS 510)

Trade Names: Emerald, Endura, and Pristine

Chemical Class: Carboxamide aka anilide

EPA Chemical Code: 128008

Chemical Abstracts Service (CAS) Number: 188425-85-6

Year of Initial Registration: 2003

Pesticide Type: Fungicide

U.S. Producer: BASF

Use Pattern and Formulations

Boscalid is a fungicide consisting of two formulated end-use products for use on food crops. The wettable granule (WG) Endura Fungicide contains 70% active ingredient, and the wettable granule (WG) Pristine contains a mixture of boscalid (25.2% active) and pyraclostrobin (12.8% active). Endura™ is intended for use on beans, berries, bulb vegetables, canola, carrots, fruiting vegetables, grapes, lettuce, peanuts, pistachios, potatoes, stone fruit, strawberries, tree nuts, *Brassica* vegetables (subgroups 5A and 5B), cucurbit vegetables, mint, edible peas, certain root vegetables, and sunflower. Pristine™ is intended for use on berries, bulb vegetables, carrots, grapes, pistachios, stone fruit, strawberries, and tree nuts. Application is via multiple, foliar, broadcast sprays at a seasonal rate of ca 0.9-1.8 lbs ai/A, depending on crop and target disease. Typically, retreatment intervals are 1-3 weeks and minimum PHIs are 0-30 days.

There is also a formulated 70% wettable granule end-use product named Boscalid Turf Fungicide for use on golf course turfgrass. No other residential uses have been proposed.

Science Findings

Summary Science Statement

The Agency has completed its review of the product chemistry, toxicology, residue chemistry, occupational exposure, ecological effects and environmental fate data submitted in support of the registration of boscalid.

The toxicology data base for boscalid is adequate to support the requested field use registrations and tolerances. There is high confidence in the hazard endpoints and dose-response assessments conducted for this chemical.

Boscalid is classified as "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". Therefore, a cancer risk assessment is not required.

The Agency has considered available information on boscalid's toxicity, potential use areas, fate properties, and application methods in characterizing ecological risks related to labeled use. Boscalid is persistent, it has low mobility in soil; however, boscalid may move to surface water through spraydrift and runoff of soil and suspended sediments. The degree of surface water contamination is mitigated by the relatively low seasonal application rates (2.1 lbs ai/acre/season) and its tendency to sorb to soil and sediment. The compound does not bioaccumulate appreciably in fish (BCF 35X-105X).

The fungicide is practically nontoxic to terrestrial animals and is moderately toxic to aquatic animals on an acute exposure basis. Boscalid acute risk quotients (RQs) do not exceed acute risk levels of concern and is not likely to pose an acute risk to animals at the maximum use rate. The RQ is not an absolute estimate of the likelihood, magnitude, or severity of risk. Inputs into this screening level assessment were designated to overestimate likely exposures and effects of boscalid. Given the slight exceedences of the RQs and the label limitations that will be imposed for boscalid, the Agency believes that potential ecological risks are low.

Physical/Chemical Properties

Physical and Chemical Properties for Technical Grade Active Ingredient

Requirement	Result
Color/Physical State	White powder (TGAI); White crystalline (PAI)
Odor	TGAI - faint smoky PAI - odorless
Stability	The test substance was found to be stable at RT and 54C for 14 days. The test substance was also found to be stable when exposed to metals like AI, & Fe, and to corresponding acetate ions.
Oxidation/Reduction	It reacts very weakly with potassium permanganate but does not react with iron, water or the fire extinguishing agent monoammonium phosphate (MAP). It is a very

	weak reducing agent.
Flammability	.Not applicable
Explodability	Non-explosive
Storage Stability	Not required for a TGAI. Accelerated storage at 54° C, in glass: day 0 - 98.16%, day 30 - 97.96.
Miscibility	.Not applicable
Corrosion Characteristics	The test substance is not expected to be corrosive to the commercial storage container
pH	5.5 at 23°C (1% solution)
Viscosity	.Not applicable
Melting Point/ Melting Range	143.4-143.6E C (TGAI); 142.8-143.8EC (PAI)
Density	1.394 g/cm^3 (TGAI); 1.381 g/cm^3 (PAI)
Dissociation Constant in Water	Test substance does not dissociate
Partition Coefficient (Octanol/Water)	log P o/w = 2.96; P o/w = 915 @ 21°C
Solubility:	PAI at 20°C in acetone (16-20 g/100 ml); acetonitrile (4-5 g/100ml); methanol (4-5 g/100 ml); ethylacetate (6.7-8 g/100 ml); dichloromethane (20-25 g/100 ml); toluene (2-2.5 g/100 ml); 1-octanol (<1 g/100 ml; water, 6 mg/L@20 C)
Vapor Pressure	7 x 10^{-9} hPa (PAI at 20°C); 2 x 10^{-8} hPa (PAI at 25°C)

Toxicological Characteristics:

Acute Toxicity Profile - Boscalid Technical

Test Material	GDLN	Study Type	MRID	Results	Tox Category
Technical	870.1100	Acute Oral - rat	45404814	LD_{50} > 5000 mg/kg	IV
Technical	870.1200	Acute Dermal - rat	45404815	LD_{50} > 2000 mg/kg	III
Technical	870.1300	Acute Inhalation	45404816	LC_{50} (M & F): > 6.7 mg/L	IV
Technical	870.2400	Primary Eye Irritation	45404817	Not irritating to the eye	IV

Technical	870.2500	Primary Dermal Irritation	45404818	Not irritating to the skin	IV

Technical	870.2600	Dermal Sensitization	45404819	Study unacceptable as challenge dose was inadequate	N/A

Toxicity Profile of Boscalid Technical.

Guideline No.	Study Type	Results
870.3100	90-Day oral toxicity rodents (rats)	**NOAEL**: 34/159 mg/kg/day (M/F) **LOAEL**: 137/395 mg/kg/day (M/F): M = increases in absolute and relative thyroid weights and increased incidence of thyroid hyperplasia as well as follicular epithelial hypertrophy; F = increases in absolute and relative thyroid weights.
870.3100	90-Day oral toxicity rodents (mice)	**NOAEL**: 197/2209 mg/kg/day (M/F) **LOAEL**: 788/2209 mg/kg/day (M/F): M = increased liver weights and increased incidence of marked fatty change in the liver; F = not attained
870.3150	90-Day oral toxicity in nonrodents (dogs)	**NOAEL**: 7.6/8.1 mg/kg/day (M/F) **LOAEL**: 78.1/81.7 mg/kg/day (M/F): M = increased alkaline phosphatase activity and hepatic weights; F = increased alkaline phosphatase activity and hepatic weights.
870.3200	21/28-Day dermal toxicity (rats)	**NOAEL**: 1000 mg/kg/day (HDT) **LOAEL**: >1000 mg/kg/day
870.3700	Prenatal developmental in rodents (rats)	**Maternal NOAEL**: 1000 mg/kg/day **Maternal LOAEL**: cannot be established **Developmental NOAEL**: 1000 mg/kg/day **Developmental LOAEL**: cannot be established
870.3700	Prenatal developmental in nonrodents (rabbit)	**Maternal NOAEL**: 300 mg/kg/day **Maternal LOAEL**: 1000 mg/kg/day based on abortions or early delivery. **Developmental NOAEL**: 300 mg/kg/day **Developmental LOAEL**: 1000 mg/kg/day based on abortions or early delivery.
870.3800	Reproduction and fertility effects (rat)	**Parental systemic NOAEL**:112.6/1180.8 mg/kg/day (M/F) **Parental systemic LOAEL**:1165.0/>1180.8

		mg/kg/day (M/F) decreased body weight and body weight gain (F_1) as well as hepatocyte degeneration F_0 and F_1) in males only. **Offspring systemic NOAEL**:11.2/115.8 mg/kg/day (M/F) **Offspring systemic LOAEL**:112.6/1180.8 mg/kg/day (M/F): decreased body weight for F_2 pups in males and females of both generations. **Reproductive NOAEL**:1165.0/1180.8 mg/kg/day (M/F) **Reproductive LOAEL**:>1165.0/1180.8 (M/F)
870.4100a	Chronic toxicity rodents (rat)	**NOAEL**: 21.9/30.0 mg/kg/day (M/F) **LOAEL**: 110.0/150.3 mg/kg/day (M/F): M = thyroid toxicity (weights and microscopic changes); F = thyroid toxicity (weights and microscopic changes). Thyroid follicular cell adenomas: M = 0/20, 0/20, 2/20,1/20; F = 0/20, 0/20, 1/20,0/20.
870.4100	Chronic toxicity dogs	**NOAEL**: 21.8/22.1mg/kg/day (M/F) **LOAEL**:57.4/58.3 mg/kg/day (M/F): M = elevated ALP activities and elevated hepatic weights; F = no effects
870.4200	Carcinogenicity rats	**NOAEL**: 23.0/29.7 mg/kg/day (M/F) **LOAEL**: 116.1/155.6 mg/kg/day (M/F): M = increased incidence of thyroid follicular cell hyperplasia and hypertrophy; F = decrease in body weight gain and increased incidence of thyroid follicular cell hyperplasia and hypertrophy. Thyroid follicular cell adenomas: M = 0/50, 0/50, 1/50, 4/50; F = 0/50, 1/50, 0/50, 3/50.
870.4200	Carcinogenicity mice	**NOAEL**:65/443 mg/kg/day (M/F) **LOAEL**: 331/1804 mg/kg/day (M/F): M = decreases in body weight and body weight gains; F = decreases in body weight and body weight gains. No evidence of carcinogenicity.
870.4300	Chronic feeding/Carcinogenicity rat	See 870.4100a and 870.4200.
870.5100	Gene Mutation bacterial reverse mutation assay	Negative without and with S-9 activation up to limit dose of 5000 µg/plate.
870.5300	*In vitro* mammalian cell forward gene mutation assay (CHO cells/HGPRT locus)	Negative without and with S-9 activation up to the limit of solubility of 25 µg/mL.
870.5375	*In vitro* mammalian cytogenetics assay in Chinese hamster V79 cells	Negative without and with S-9 activation up to 3500 µg/mL with precipitation showing at concentrations of 100 µg/mL and higher.

870.5395	Cytogenetics - mammalian erythrocyte micronucleus test in the mouse	Negative at doses up to 2000 mg/kg.
870.5500	*In vitro* unscheduled DNA synthesis (primary rat hepatocytes)	Negative response up to 50 µg/mL. Cytotoxicity at 100-500 µg/mL.
870.6200	Acute neurotoxicity screening battery (rat)	**NOAEL**:2000/1000 mg/kg/day (M/F) **LOAEL**: >2000/2000 mg/kg/day (M/F): F = piloerection
870.6200	Subchronic neurotoxicity screening battery (rat)	**NOAEL**:1050.0/1272.5 mg/kg/day (M/F) **LOAEL**: >1050.0/1272.5 mg/kg/day (M/F)
870.6300	Developmental neurotoxicity (rat)	**Maternal NOAEL:**1442 mg/kg/day **Maternal LOAEL:** >1442 mg/kg/day **Offspring NOAEL:** 14 mg/kg/day **Offspring LOAEL:** 147 mg/kg/day (decreased body weights on PND 4 and decreased body weight gain on PNDs 1-4)
870.7485	Metabolism and pharmacokinetics (rat)	Boscalid was readily absorbed and excreted following single oral 50 mg/kg; at single 500 mg/kg or 15 doses of 500 mg/kg, absorption was saturated. Excretion mainly by feces (80-98%). Biliary excretion 40-50% of fecal activity at 50 mg/kg, 10% at 500 mg/kg. Urine, about 16% at 50 mg/kg, 3-5% at 500 mg/kg. Absorption about 56% at 50 mg/kg and 13-17% at 500 mg/kg. Excretory patterns similar by gender or radiolabel position. Metabolites (hydroxylation and conjugation products) were consistent with Phase I oxidation reactions followed by Phase II conjugation with glucuronic acid or sulfate, or by conjugation of the parent with glutathione with cleavage to sulfate metabolites.
870.7600	Dermal Penetration (rat)	Maximum % absorption: 0.01 mg/cm^2 = 10.93 (24 hour exposure, 24 hour sacrifice) 0.10 mg/cm^2 = 3.76 (24 hour exposure, 24 hour sacrifice) 1.00 mg/cm^2 = 1.48 (10 hour exposure, 72 hour sacrifice)
none	SPECIAL STUDY: Hepatic enzyme induction (rat)	1. hypertrophy of zone III hepatocytes 2. >20% increase in liver weight 3. increase in CYP450 activity 4. slight to extensive microscopic SER proliferation 5. not a peroxisome proliferator

		6. enzymes in CYP450 subfamily not induced 7. no notable microscopic increase in size or number of peroxisomes CONCLUSION: inducer of total CYP450 activity
none	SPECIAL STUDY: Hormone and enzyme induction (rat)	1. slight (statistically significant) decrease in circulating T_3 and T_4 only in males 2. increase in circulating TSH levels both sexes 3. increase in all 3 liver microsomal glucuronyltransferases CONCLUSION: disruption of thyroid homoeostasis by decreasing circulating T_3 and T_4 and increasing TSH; likely the result of hepatic microsomal glucuronyltransferase induction
none	SPECIAL STUDY: Reversibility study (dietary): 4-week administration followed by 4 weeks recovery or 13 weeks recovery (rat)	4 weeks dosing: at 2500 and 15000 ppm: increase in TSH (68% and 87%); increase in absolute and relative thyroid weights, hypertrophy of thyroid follicular epithelial cells and diffuse follicular hyperplasia, increase in absolute and relative liver weights and centrilobular hypertrophy as well as liver portal fatty changes. 4 weeks dosing + 4 weeks recovery: no increases in TSH; increase in absolute and relative thyroid weights; thyroid hypertrophy and hyperplasia decreased to control values; all liver effects reversed to control. 4 weeks dosing + 13 weeks recovery: no increases in TSH; increase in absolute and relative thyroid weights; thyroid hypertrophy and hyperplasia decreased to control values; all liver effects reversed to control. CONCLUSION: induction of liver microsomal enzyme system resulting in increased glucuronidation of thyroxine, resulting in an increase in TSH secretion as a compensatory response of the physiological negative feedback system; increased TSH resulted in increased thyroid weight.

Summary of Toxicology Findings.

Boscalid has a low toxicity (toxicity categories III or IV for oral, dermal, inhalation, primary eye irritation and primary skin irritation). In a dermal sensitization study in guinea pigs, the study was unacceptable because the concentration used for the challenge was inadequate.

In subchronic and chronic feeding studies in rats, mice and dogs, boscalid generally caused decreased

body weights and body weight gains (primarily in mice) and effects on the liver (increase in weights, changes in enzyme levels and histopathological changes) as well as on the thyroid (increase in weights and histopathological changes).

In a developmental toxicity study in rats, no developmental toxicity was observed in the fetuses at the highest dose tested (Limit Dose). No effects were noted in the dams in this study. In a developmental toxicity study in rabbits, an increased incidence of abortions or early delivery was observed at the Limit Dose. Since it could not be determined whether the abortions or early delivery were due to maternal toxicity or due to an effect on reproductive/developmental mechanisms, the LOAELs and NOAELs in this study for both maternal and developmental toxicity were considered to be the same. The does (maternal toxicity) and fetuses (developmental toxicity) were considered to be equally sensitive to the test material. This study does not indicate an increased susceptibility of fetuses, as compared to does. In a 2-generation reproduction study in rats, the NOAEL for parental toxicity was based on decreased body weight and body weight gain as well as hepatocyte degeneration. The NOAEL for offspring toxicity was based on decreased body weights and body weight gains for the pups. No reproductive toxicity was observed in this study at the highest dose tested. There was no evidence of susceptibility in the developmental rat study. There was evidence of qualitative (not quantitative) susceptibility in the developmental rabbit study as characterized by an increased incidence of abortions or early delivery at the highest dose tested. There was quantitative evidence of increased susceptibility in the two-generation reproduction study in rats, where decreases in body weights and body weight gains in male offspring were seen at a dose that was lower than the dose that induced parental/systemic toxicity. There was quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats, where decreases in pup body weights (PND 4) and body weight gains (PND 1-4) were seen in the absence of any maternal toxicity.

In a two-year chronic toxicity study and a two-year carcinogenicity study in male and female rats, the combined data showed that, for thyroid follicular cell adenomas, males had a significant increasing trend and significant differences in the pair-wise comparison of the highest dose group, when compared with controls. There was no treatment-related increase in thyroid follicular cell carcinomas. The increased incidence of the thyroid follicular cell adenomas exceeded the historical control mean and range. The increase in thyroid follicular cell adenomas appeared to be treatment-related in males. This was supported by thyroid hypertrophy and hyperplasia of follicular cells at the same dose as well as increased thyroid weights plus mechanistic data. Regarding females, combined data from the two rat studies indicated that there was an increasing trend for thyroid follicular cell adenomas which appeared to be treatment related. No carcinomas were observed in females. Boscalid is classified as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", according to the EPA *Draft Proposed Guidelines for Carcinogen Risk Assessment* (July 2, 1999).

Boscalid (BAS 510 F) was tested in five mutagenicity studies and was found to be negative in all of them.

In neither an acute nor a subchronic neurotoxicity study in rats was there evidence of a neurotoxic effect at the Limit Dose. In a developmental neurotoxicity study in rats, there were no neurotoxic effects observed at the Limit Dose. No neurotoxic observations were noted in any of the other studies in any species.

In metabolism and pharmacokinetic studies, Boscalid was readily absorbed and excreted following a single oral dose of 50 mg/kg. At single 500 mg/kg or 15 doses of 500 mg/kg, absorption was saturated. Excretion was mainly by feces (80-98%). Biliary excretion was 40-50% of fecal activity at 50 mg/kg and 10% at 500 mg/kg. Urinary content was about 16% at 50 mg/kg and 3-5% at 500 mg/kg. Absorption was about 56% at 50 mg/kg and 13-17% at 500 mg/kg. Excretory patterns were similar by gender or radiolabel position. Metabolites (hydroxylation and conjugation products) were consistent with Phase I oxidation reactions followed by Phase II conjugation with glucuronic acid or sulfate, or by conjugation of the parent with glutathione with cleavage to sulfate metabolites.

A dermal absorption study in rats is available. Doses used were 0.01, 0.10 and 1.0 mg/cm^2. The maximum percent absorptions were as follows: 0.01 = 10.93 (24 hour exposure, 24 hour sacrifice); 0.10 = 3.76 (24 hour exposure, 24 hour sacrifice); and 1.00 = 1.48 (10 hour exposure, 72 hour sacrifice). The total amount of absorption was 15% as represented by 11% being absorbed at 24 hours plus 4% found as bound residue on the skin.

Occupational and Residential Exposure and Risk Characterization.

All MOEs for the handlers performing agricultural crop uses were greater than the target of 100 at the baseline level (ranging from 460 to 31,000). All MOEs for the handlers performing golf course turfgrass uses were also greater than the target of 100 at the baseline level (ranging from 7,300 to 27,000).

The handler exposure estimates in this assessment are based on a central tendency estimate of unit exposure and an upper-percentile assumption for the application rate, and are assumed to be representative of high-end exposures. The uncertainties associated with this assessment stem from the use of surrogate exposure data (e.g., differences in use scenario and data confidence), and assumptions regarding that amount of chemical handled. The estimated exposures are believed to be reasonable high-end estimates based on observations from field studies and professional judgement.

The Agency uses the term “post-application” to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. There are two recreational scenarios associated with boscalid that could lead to exposures for adults and children: 1.) golfing and 2.) picking their own fruit. These exposure durations are anticipated to be short-term (golfing) or acute (one day for picking fruit). Because “pick your own fruit” is considered a “one-time” event (duration <1 day) and oral studies indicated there were no toxicological endpoints appropriate to quantitate acute risk, this exposure scenario was not evaluated.

The boscalid label specifies that this product is intended for golf course use only, and not for use on residential turfgrass or turfgrass being grown for sale or other commercial use such as sod production. Although the label does not indicate that the product is applied by licenced or commercial applicators, it is acknowledged that the homeowner will not be applying the product to golf courses. Therefore, a risk assessment for residential handler exposure is not required.

FQPA CONSIDERATIONS

The special FQPA safety factor is reduced to 1X because the existing data indicate that there are no/low concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity.

Conservative residue assumptions are used in the dietary risk assessments; there are no uses that will result in residential exposure except golf course and pick-your-own fruits; and the residue chemistry and environmental fate databases are relatively complete (evaluated by the risk assessment team). A 1X database factor is to be applied to all dietary and residential exposure endpoints as there are no data gaps. The Agency selected endpoints for chronic dietary exposure (all populations), incidental oral short- and intermediate-term residential only, dermal (all durations) and inhalation (all durations). As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD). For all of the endpoints selected, liver and thyroid effects were chosen from the chronic toxicity study in rats, the carcinogenicity study in rats and the 1-year study in dogs. The NOAEL was 21.8 mg/kg/day. The uncertainty factor (UF) was 100. For the dermal route, the absorption rate was 15% relative to oral. For the inhalation route, the absorption rate was assumed to be 100%. The cPAD for the chronic dietary (all populations) exposure scenario = 0.218 mg/kg/day. The residential and occupational level of concern (LOC) is MOE = 100 for all routes (i.e., margins of exposure < 100 are of concern).

Exposure Scenario	Dose	Endpoint	Study/Effect
Acute dietary	No appropriate endpoint identified	none	not applicable
Chronic dietary (all populations)	NOAEL = 21.8 mg/kg/day	cRfD and cPAD = 0.218 mg/kg/day	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Incidental oral (short- and intermediate-term residential only)	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential and occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Dermal (all durations) Absorption: 15%	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential), 100 (occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Inhalation (all durations) Absorption: 100%	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential), 100 (occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.

Aggregate Exposure And Risk Characterization

Aggregate exposure risk assessments were performed for short term and chronic aggregate exposure. Short term and chronic aggregate exposures take into account dietary (food + drinking water) and residential exposures. Since the Agency does not have ground and surface water monitoring data to calculate a quantitative aggregate exposure, drinking water levels of comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxic endpoint, drinking water consumption, body weights, and pesticide uses. Different populations will have different DWLOCs. The Agency uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

To calculate chronic DWLOCs, the dietary food estimates (from DEEM™) were subtracted from the chronic PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70kg/2L (adult male and US Population), 60 kg/2L (adult female), and 10kg/1L (infant & children).

As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD) for the general population or females 13-50 years old. An acute aggregate risk assessment is not needed.

The chronic aggregate risk assessment takes into account average exposures estimates from dietary consumption of boscalid (food and drinking water) and residential uses. Since there are no chronic residential exposures associated with uses of boscalid, the chronic aggregate included food and drinking water only. The calculated chronic DWLOCs for chronic exposure to Boscalid in drinking water range from 1400 to 7000 µg/L (ppb). EECs generated are less than the calculated chronic DWLOCs . Therefore, the chronic aggregate risk associated with the proposed use of BAS 510 does not exceed the Agency's level of concern for the general U.S. population or any population subgroups.

Post application exposures from the sue oon golf couse is considered short term and applies to adults and youth. Although, a shourt term dermal risk assessment was conducted for the adult only, the adult MOEs are also considered representative for youths playing golf since the body surface area to weight ratios for adolescents do not vary significantly from those for adults. Since all endpoints are from the same study, exposure from different routes can be aggregated . The short term aggregate risk assessment takes into account average exposures from dietary consumption of boscalid (food and drinking water) and exposures from non-occupational sources (golf course). The calculated MOE from food and non-occupational exposure is 1200, and the calculated short term DWLOC is 6000 ppb. Compared to the surface water and ground waer EECs the short-term DWLOC is considerably larger and therefore the short term aggregate risk does not exceed the Agency's level of concern.
Cancer Assessment

The Agency classified Boscalid (BAS 510 F) as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", and, therefore, the quantification of human cancer risk is not recommended. The cancer classification was based on the following weight of evidence considerations. First, in male Wistar rats, there was a significant trend (but not pair wise comparison) for the combined thyroid adenomas and carcinomas. This trend was driven by the increase in adenomas. Second, in the female rats, there was only a borderline significant trend for thyroid adenomas (there were no carcinomas). Third, the mouse study was negative as were all of the mutagenic tests. Consistent with this weak evidence of carcinogenic effects, the Agency concluded that a dose-response assessment for cancer (either linear low-dose extrapolation or margin of exposure calculation) was not needed.

Ecological Effects/Environmental Fate Characteristics:

1. Environmental Fate Summary:

Boscalid is a slowly degradable compound with low mobility in most soils. The primary degradation

pathway is aerobic soil metabolism, which proceeds slowly and results in the formation of intermediates which are relatively rapidly transformed into CO_2 or bound soil residues. The majority of the apparent degradation of the compound is actually due to its transformation to bound residues. Degradates of the compound include 2-chloronicotinic acid (M510F47), 2-hydroxy-N-4'-chlorobiphenyl-2-yl)-nicotinamide (M510F49), and an unknown (M5100F50). Boscalid is hydrolytically stable and is photolytically stable on soil and in water. The compound is not transformed to any significant extent in either aerobic or anaerobic aquatic systems, but is relatively rapidly transferred (dissipation half-lives of <2 weeks) from the water phase to the sediment phase of sorbing to the sediment.

Boscalid has low mobility in most soils, as it tends to sorb to the organic matter. As such, it is likely to sorb to aquatic sediments. Data from batch equilibrium studies, when considered along with results from Tier 1 computer models and terrestrial field dissipation studies, indicate a low potential for leaching. A slightly higher potential for leaching exists for the compound in soils which are low in organic matter content, is as often the case with coarse-textured soils. There is a potential for Boscalid to reach surface water through spray drift when applied using ground spray (multiple crops) or aerial spray (canola). The potential for overland surface runoff of the compound in the water phase is low, although it may occur due to the aqueous solubility of the compound. However, because Boscalid is generally persistent under field conditions, over time the compound may be present in field runoff as a sorbed residue, and limited desorption of the bound parent compound from soil particles may occur in surface water bodies, particularly in soils with low organic matter content. The slow biodegradation of Boscalid in most soils will increase the potential for both groundwater and surface water contamination. However, the potential for groundwater contamination should be mitigated by the tendency of the compound to adsorb to surface soils, particularly those with relatively higher levels of organic matter. The potential for boscalid to leach in significant quantities or to reach surface water will be mitigated by the low application rate ($\leq$21b. a.i./A/season. Because boscalid does not biodegrade in aquatic systems, but does bind to sediments, the compound is expected to accumulate in the sediment phase of these environments. Results from Tier 1 models indicate that concentrations of Boscalid will be relatively low in groundwater and surface water, but that the compound will accumulate in surface water bodies. The boscalid degradate 2-chloronicotinic acid is very mobile in soil and is not expected to bind to aquatic sediments. However, the degradate is metabolized rapidly in aerobic soil, and is mineralize to CO_2 or tranformed to bound residues.

a. Hydrolysis

Boscalid is stable to hydrolysis at environmentally relevant pHs and temperature. Uniformly diphenyl ring-labeled [^{14}C]Boscalid, at 3 mg a.i./L (ppm) in sterile aqueous buffer solutions maintained at 25^{o}C for 30 days, was stable to hydrolysis at pH 5, 7 and 9. Based on the results obtained at 25^{o}C the parent compound is not expected to hydrolyze in the environment, rendering hydrolysis an insignificant fate process for boscalid.

b. Photolysis

Boscalid is stable to photolysis in water. Pyridine ring-labeled [3-^{14}C]Boscalid, at 3 µg a.i./mL (ppm), was stable to photolysis in sterile pH 5 (acetate) aqueous buffer solutions maintained at 22 $\pm$ 1^{o}C under continuous irradiation (xenon lamp) for 15 days. Based on the results of the study, photodegradation is not expected to be a significant route of dissipation for boscalid in the environment.

Boscalid is stable to photodegradation on soil. Pyridine ring-labeled [3-^{14}C]Boscalid, at 4.6 µg a.i./g soil (ppm), was stable to photodegradation on a standard (laboratory mix) German sandy loam soil (pH 7.3, organic carbon 1.9%) that was continuously irradiated (xenon lamp) while maintained at 22 $\pm$ 1°C and 40% of maximum water holding capacity for 15 days. Based on the results of the study, photodegradation is not expected to be a significant fate processor boscalid in the environment.

c. Metabolism

Boscalid is metabolized slowly in aerobic soils, while its degradate 2-chloronicotinic acid is metabolized rapidly in such soils. The biodegradation of boscalid (diphenyl and pyridine labels) was studied in multiple soils. The degradation of boscalid in aerobic soils was slow, with half-lives ranging from 96 to 578 days. It is noted, however, that the majority of the compound's apparent degradation is actually due to its transformation to bound residues rather than to actual degradation or complete mineralization of the compound.

Boscalid is degraded very slowly in anaerobic soils used on data obtained from two studies (diphenyl and pyridine labels) conducted using a standard (laboratory mix) German soil. Valid half-lives could not be determined in either study since the degradation of boscalid did not reach 50% of the applied by the end of the study periods (120 days). For assessment purposes, boscalid may be considered to be essentially stable to microbial degradation in anaerobic soils, as the disappearance of the parent compound was mainly due to bound residues, i.e., sorption, and no major degradates were detected.

d. Sediment/Water Systems

Boscalid is stable in anaerobic aquatic systems. Pyridine ring-labeled [^{14}C]Boscalid and uniformly diphenyl ring-labeled [^{14}C]Boscalid, at respective rates of 0.27 and 0.26 mg a.i./L, were metabolically stable in pond water/clay loam sediment systems (1:2 w:v;water pH 8.4; soil pH 7.3, organic matter 4.9%) from North Dakota, which were maintained at 20 $\pm$ 1°C under a nitrogen atmosphere for 361 days. In the water phase, [^{14}C]Boscalid decreased from 92.2-94.5% of the applied at day 0 to 50.9-53.1% by 7 days, and 9.6-14% by 35 days and 3.6 days and 3.6-4.6% by 361 days. In the sediment phase [^{14}C]Boscalid increased to a maximum of 59.1-61.9% by 35 days, then slowly decreased to 44.16-44.2% by 361 days. In total sediment:water system, [^{14}C]Boscalid decreased from 92.2-94.5% of the applied at day 0 to 49.7-51.8% at 179 days and 46.2-47.8% at 361 days. The calculated half-life (first-order linear) for the combined data was 385 days; DT50 (nonlinear) was 302-342 days. However, degradation was not observed, and the reported half-life is not true metabolic half-life. Disappearance of the parent was attributed to sediment binding. Residues partitioned to the soil with time; water:sediment and residue distribution were 1.2:1 at 7 days, 1:5 at 362 days; the vast majority of the bound residues were associated with the humin fraction of the soil organic matter. Volatiles were negligible.

Boscalid is stable in aerobic aquatic systems. Pyridine ring-labeled [^{14}C]Boscalid and uniformly diphenyl ring-labeled [^{14}C]boscalid, at 0.24 mg a.i./L, were metabolically stable in a water/German loamy sand sediment system (1:1.5, w:v; water pH 8.50, organic carbon 12.0-14.4 a pH in Ca $C1_2$ 6.8, organic carbon 0.8%) from a pond in Germany, an a water/German loam sediment system (1.2.1, w:v; water pH 8.10, organic carbon 8.6-15.2%; sediment pH in $CaC1_2$ 7.5, organic carbon 4.1-4.3%) from a pond-like area adjacent to a river in Germany, which were maintained at 20$\pm$ 2°C for 100 days. Aerobic conditions were maintained in the water layer f the

water/sediment systems, but the sediment layer remained anaerobic throughout the study. Total [^{14}C] residues of [^{14}C]Boscalid (both labels) gradually partitioned from the water layer to the loamy sand sediment with distribution ratios (water:sediment) of ca. 4:1 at day 1, 1:1 at 7-14 days, 1:2 at 29 days and 1:5 at 100 days but, in comparison, partitioned from the water layer to the loam sediment more rapidly, with distribution ratios of ca. 2:1 at day 1, 1:1 at 2 days, 1:2 at 7 days, 1:7 at 29 days and 1:15 at `100 days. No major degradates were detected in any of the systems. Non-extractable [^{14}C] residues in both sediments were 10.3-13.4% at 100 days. Volatiles were negligible. Boscalid was stable in all water/sediment systems, with dissipation of parent compound from the water layer to the sediment. Half-lives were not calculated for the total systems since degradation of the parent was negligible.

e. Mobility

Based on K_{oc} values and the McCall classification scheme (Swann et al., 1983), boscalid is expected to have low mobility in most soils and expected to bind to aquatic sediments. The adsorption of boscalid was assessed in two foreign soils (German standard soils; laboratory mixes), two U.S. soils and one Canadian soil at 22 $\pm$ 1°C in batch equilibrium studies using a 23-hour adsorption phase; desorption of the compound was assessed using a 16-hour desorption phase.

The boscalid degradate 2-chloronicotinic acid (M510F47) is expected to be very mobile in soil and is not expected to bind to aquatic sediments. The adsorption of the compound was assessed in three U.S. soils at 21°C in batch equilibrium studies using a 24-hour adsorption phase; desorption of the compound was assessed using a 16-hour desorption phase.

f. Field Dissipation

Based on terrestrial field dissipation studies, boscalid is generally persistent in the field, both in bare and cropped plots. The terrestrial field dissipation of boscalid was studied at several U.S. sites on various cropped and bare ground plots, and on bare ground plots in Canada.
The DT_{50}'s for dissipation of the parent compound from the surface solid for boscalid applied to bare ground plots (U.S. and Canada) ranged from 27 to 372 days (with the exception of a DT_{50} of 1 day which was of questionable validity due to data variability), and were generally greater than 100 days and frequently greater than 200 days. The residue carryover as a percentage of the total application range of 11.9-52.3% for the bare ground plots. The DT_{50}'s for dissipation of the parent compound from the surface soil for boscalid applied to cropped plots (U.S. only; turf, peach, almond) ranged from 44 to >360 days and were generally greater than 100 days. The residue carryover as a percentage of the total application was a range of 6.2-20.1% for the cropped plots. The maximum mean concentrations of the degradate M510F49 ranged from 0.01 mg/kg to 0.04 mg/kg across all studies. The maximum mean concentrations of the degradate M510F47 ranges from 0.003 mg/kg to 0.04 mg/kg across all studies.

g. Bioaccumulation

Boscalid is expected to accumulate in fish tissues at moderate levels, with greater accumulation in the nonedible tissue versus the edible tissue, but should depurate rapidly from the tissues when the fish are no longer exposed to the compound.

2. Ecological Risk Summary

a. Risk to Aquatic Organisms

Exposure to aquatic communities is expected to be limited due to the chemical's tendency to sorb to sediments. Boscalid is moderately toxic to aquatic animals; however based on estimated exposure concentrations, the proposed uses of boscalid are not likely to represent a threat to either acute or chronic ecological risk to freshwater fish and invertebrates or to estuarine/marine fish at a maximum proposed multiple application rates as high as six applications of 0.350 lbs. a.i./A. However, the acute risk level of concern for endangered species is exceeded for estuarine/marine invertebrates. While boscalid is not expected to adversely affect aquatic animals whose lives are primarily spent in open water, bottom-dwelling (benthic) fauna may be more likely to encounter boscalid based on the chemical's persistence and tendency to sorb to sediments. Modeling of benthic exposure, based on a closed farm pond scenario over a 36-year period, did not exceed the chronic risk level of concern for sediment-dwelling animals.

b. Risk to Avian Species (Acute/Chronic)

Boscalid is categorized as practically nontoxic to birds n both an acute and subacute exposure basis, no acute levels of concern (LOC) are exceeded for birds feeding on any of the modeled food items (short grass, tall grass, broadleaf plants insects and seeds). However, chronic exposure to boscalid at the proposed application rate for strawberries, i.e., 5 applications of 0.350 lbs a.i./A with a 7-day reapplication interval, results in the chronic risk level of concern being exceeded for birds feeding on short grasses (RQ=1.08). Exposure to boscalid on other avian food items (tall grasses, broadleaf plants/insects, and seeds) at this application rate did not result in any exceedance of either acute or chronic LOCs. Based on maximum estimated concentrations on short grass the chronic risk LOC would be exceeded for approximately 4 days; however, if mean foliar residues were used to estimate exposure, chronic avian LOCs would not have been exceeded since mean foliar residues are roughly half maximum exposure values.

c. Risk to Mammalians (Acute/Chronic)

Boscalid is practically nontoxic (LD_{50}>5,000 mg/kg) to rats on an acute exposure basis. Chronic toxicity data provided through a 2-generation rat production study indicated that decreased body weight and decreased body weight gains in F_2 males pups (NOAEC=100 ppm).

d. Risk to Plants

Ecological effects testing on a range of terrestrial and semi-aquatic plants revealed that the detrimental effects for all the test endpoints were less than 25% when compared with the pooled control. As a result, the EC_{25} was greater than 0.55 lb a.i./A. Therefore, RQ values have not been calculated for terrestrial and semi-aquatic plants and it is assumed that at rates less than or equal to 0.55 lbs/A, boscalid use does not represent a risk to plants.

DATA NEEDS

Label Restrictions

1. The Endura and Pristing labels must include a statement that use is prohibited on soybean, cowpea, field pea, and lupin; sugar beets, garden beets, turnips, and radishes.

2. Recropping (Plantback) Restrictions: The Endura™ and Pristine™ Fungicide labels must include a

statement that: "Crops with registered uses may be replanted at any time. All other crops grown for food or feed may be replanted after 14 days."

3. Maximum Seasonal Use Rate: As a precautionary measure, the Endura™ and Pristine™ Fungicide labels must include a statement to the effect that, if ever both these formulated products should be applied interchangeably to the same crop (i.e., same plants) during the growing of that crop, the total amount of ai/A applied to that crop must not exceed that allowed had only one of these formulated products been used (i.e., ca 0.9-1.8 lbs ai/A total per season, depending on the specific crop).

There are also several **conditions of registration** associated with the granting of these tolerances:

! Conditions of Registration

860 Series - Residue Chemistry
- Completion of Agency method validations
- Radiovalidation data demonstrating extraction efficiency of methods
- Storage stability - final plant report and data for grape juice and tomato paste
- Additional field trials for mustard greens, cucumbers and sunflower seed
- Field rotational crop data for best and turnip tops, spinach, and celery

Environmental Fate and Effects

Data Gap

1. Aquatic toxicity tests using fish and invertebrates were classified as supplemental since water quality parameters did not adherer to standards recommended by the Agency. If the registrant can demonstrate that pH, water hardness and the use of dechlorinated tap water do not affect the toxicity of boscalid and if it can be demonstrated that mean measured concentrations accurately reflect the amount of chemical in solution, these studies can be upgraded to core.

2. Submission of a freshwater invertebrate life cycle study - non of the required data are provided on growth (length and weight) of Daphnia magna. If registrant has these data, they should provide for review, otherwise the Agency recommends that the study be repeated.

3. Submission of the toxicity data must be provided for freshwater mollusc such as *Corbicula spp.*, given the persistence of boscalid and its tendency to partition on to sediments.

Label Language:

Surface Water Advisory:

"This product may contaminate water through drift spray in wind. This product has a potential for runoff according to the pesticide's "mean" soil partition coefficient (15 mgL/g^2) for several months or more after application. Poorly draining soils and soils with shallow water tables are more prone to produce runoff that contains this product. A level, well maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential for contamination of water from rainfall-runoff. Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours."

Contact person at USEPA

Mailing address

Cynthia Giles-Parker
Product Manager (22)
Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505C)
Fungicide Branch
1200 Pennsylvania Avenue NW
Washington, D.C. 20460

Office location and telephone number:

Room 249, Crystal Mall #2
1921 Jefferson Davis Highway
Arlington, VA 22202
703-305-7740

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